

Breast Cancer Vaccine: Are We There Yet?

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Editorial

Breast cancer is the most fatal form of cancer for female population worldwide. National Cancer Institute (NCI) estimates 226,870 females and 2,190 males to be diagnosed with breast cancer in the United States by the end of 2012. The estimated death toll for this year includes 39,510 females and 410 males, as reported by NCI. Statistics state that 1 in every 8 females will be diagnosed with breast cancer during her lifetime. These alarming numbers have provoked a large number of scientists to contribute towards the fight against breast cancer. Today there are various tools available for females to protect them from breast cancer. Mammography serves as an efficient tool in screening and catching such cases early enough for improved treatment, while surgery, radiotherapy and chemotherapy provide a strong line of treatment to breast cancer patients. Cancer patients are often subjected to a combination of such therapies, leading to cumulative adverse effects accompanied with the treatment. Addressing the growing number of breast cancer cases, the adverse effects associated with current therapies and the risk of having a relapse after undergoing extensive conventional therapy, researchers are now looking forward for a breast cancer vaccine [1-3].

So far vaccines have been very effectively employed to prevent the infectious diseases, but the role of vaccines against cancer still remains to be explored. Infectious diseases are caused by pathogens, which are foreign in origin and thus immunizing the body to recognize these non-self invaders is relatively a less daunting task. However, cancer originates by uncontrolled growth of own cells, thus immunizing the body against such self-antigens is a challenge. This strongly correlates with the fact that we have only one US Food and Drug Administration (FDA) approved cancer vaccine available to us currently. Provenge/Sipuleucel-T (Dendreon Corporation, Washington) is the only FDA approved therapeutic cancer vaccine against prostate cancer. Which involves activation of dendritic cells in presence of a prostate cancer antigen along with an immunostimulant. This vaccine has shown a marginal increase in the life span of prostate cancer patients by on an average of four months at a cost of \$93,000. Dendreon Corporation is currently evaluating this approach to develop a breast cancer vaccine, Neuvenge/Lapuleucel-T, which uses the Human Epidermal growth factor Receptor 2 (HER 2) antigen as the immunogenic component of the vaccine b [4].

The HER 2 antigen has also been explored as the source of E75 peptide vaccine, which is currently under Phase III clinical trial. The E75 peptide/NeuVax™ vaccine is a promising clinical trial offering hope to breast and ovarian cancer patients having HER 2 positive tumors [5]. Even the patients, whose HER 2 antigen expression is low (Immunohistochemistry [IHC] score of 1+/2+) can benefit from this vaccine. Such patients could not benefit from the well-received antibody therapy of Herceptin and contributed to two-third of HER 2+ breast cancer population. NeuVax™ aims to target breast cancer survivors with healthy immune system, providing ample opportunity to the vaccine to elicit its response [3].

Several other breast cancer antigens such as Mucin 1 (MUC1), human telomerase reverse transcriptase (hTERT), tumor protein 53

(p53), and cancer embryonic antigen (CEA) have been identified and employed as vaccines as well. Thus, various researchers have explored different breast cancer vaccines in the quest of finding the one, which can benefit the breast cancer patients.

On similar lines, Chablani and D'Souza et al., proposes the preparation of breast cancer vaccines, formulated in a particulate delivery system [6]. The immune response elicited by a vaccine not only depends on the immunogenicity of the antigen, but also the mode of antigen presentation [7]. A particulate delivery system enhances the antigen presentation of such antigenic components, thus leading to an efficacious vaccine. The author has reported the use of particulate delivery system to prepare an oral murine breast cancer vaccine, which was successfully tested in a female Balb/c mice model. Oral route of vaccine administration appears to be lucrative not only due to ease of administration but also due to the availability of specialized phagocytic M-cells present in Peyer's patches of small intestine. These M-cells specialize in sampling pathogens from gut and present them to the immune cells housed beneath them [8,9]. Thus having a particulate oral breast cancer vaccine sampled by the M-cells leads to induction of both cellular and humoral immunity, as shown by the author. This oral murine breast cancer vaccine has been successfully tested as a prophylactic approach and currently the group is evaluating the efficacy of this vaccine therapeutically.

Another alternate route of administration, which has been explored for influenza vaccine, recently, is the transdermal route. The vaccine is administered via skin with the aid of micron-sized needles [10]. These microneedles, when applied on skin, painlessly create aqueous conduits, which can be used to deliver the vaccine into the epidermis. The epidermis hosts various antigen-presenting cells (Langerhans cells), which are capable of activating immune cells to generate protective immunity. Chablani and D'Souza et al. have also explored this route of administration for an efficacious particulate murine breast cancer vaccine (data not yet published). Transdermal route of breast cancer vaccination did result in a protective immune response against tumor challenge as evaluated in a prophylactic vaccine study by the Chablani and D'Souza et al.

Considering the advent of nanotechnology and the advances in the field of immunotherapy, we hope to have an efficacious breast cancer vaccine soon.

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